Amendments to the Specification begin on page 3 of this paper.

Remarks begin on page 5 of this paper.

Amendments to the Specification:

Please replace paragraph **[97]** beginning at page 26, line 20, with the following:

--**[97]** To generate melanopsin knockout mice, we replaced exon 1 of melanopsin with a neomycin gene by homologous recombination in embryonic stem cells (Figure 1A). A targeting construct was generated by cloning a 3.1kb 5' arm and a 3.2kb 3'arm of genomic DNA (Figure 1A) from a BAC clone encompassing the *Opn4* locus into a modified version of pGEM3 (Promega, Madison, WI). The targeting construct was linearized by *NotI*, and microinjected into an embryonic stem (ES) cell line from 129S1/Sv. The ES cell clones were selected on G418, and 96 positive ES cell clones were screened by PCR using primer pairs ac and df for replacement of the exon1 with neomycin resistance gene. Two clones with appropriate insertion were injected into C57/Bl6 blastocysts and introduced into C57/Bl6 pseudopregnant females. Chimeric males were mated with C57/Bl6 females. Chimeras from a single clone produced agouti coat color heterozygote animals, which were subsequently mated with C57/Bl6 mice. Heterozygote mice were interbred, and the resultant progeny were genotyped by PCR amplification. The progeny were found to have a normal 1:2:1 Mendelian segregation pattern for the $Opn4^{neo}$ allele, suggesting that *Opn4* is not required for normal viability. $Opn4^{-/-}$ mice and littermate $Opn4^{+/-}$, and $Opn4^{+/+}$ mice were used in all assays. Primer
a=CAGGAGCAAGGTGAGATGACAGGAG (SEQ ID NO:5),
b=AGGATGGTATAGAGCCGGAAGTCTG (SEQ ID NO:6),
c=TCAAGCCACAGAGGATACTAGCAGG (SEQ ID NO:7),
d=GATGATCTGGACGAAGAGCATCAGG (SEQ ID NO:8),
e=ACTGAGGACTGACACTGAAGCCTGG (SEQ ID NO:9),
f=CAGTGTCAGGCCTAGCGGGAAGAGA (SEQ ID NO:10).--

Please replace paragraph **[116]** beginning at page 33, line 13, with the following:

--**[116]** Wheel running activity was monitored in mice maintained in an 8L:16D photoperiod. Experimental groups were exposed to extended light until 9h after the predicted time of activity onset (equivalent to 9h after dark onset in those genotypes that are photoentrained). Animals were anesthetized with isoflurane, and pineals were excised and immediately placed in 10 µl of RNAlater (Ambion Inc., Austin, TX). Total RNA was extracted (RNAqueous™-Micro; Ambion Inc.) and reverse transcribed (Superscript™ II Reverse Transcriptase Preamplification System; Invitrogen, Carlsbad, CA). Relative quantities of AA-NAT mRNA were determined in a ABI PRISM GeneAmp 5700 Sequence Detection System (Applied Biosystems Inc., Foster City, CA) using SYBR Green and AA-NAT specific primers (forward, 5'-CAG CCC CCA GGA CAA CAC-3' (SEQ ID NO:11); reverse, 5'-GGT TCC CCA GCT TCA GAA GTG-3' (SEQ ID NO:12)) that span the first intron and were designed using Primer Express 1.5 software (Applied Biosystems Inc) according to the GenBank sequence accession number NM_009591.1. The presence of a single amplimer of appropriate size was confirmed by melting curve analysis.--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1-8, at the end of the application.